Notice of Allowability	Application No.	Applicant(s)	
	09/147,036	MAURER ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *1/20/06*.

2. ☒ The allowed claim(s) is/are *1, 9-15, 19, 41, 43-53 and 55-58 are allowed and have been renumbered as 1-25, respectively.*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____.
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *4/27/06*.
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

Allowance

1. This Office Action is responsive to Applicant's amendment and remarks filed January 20, 2006. Claims 2-8, 16-18, 20-40, 42, 54 and 59 have been cancelled. Claims 1, 9-15, 19, 41, 43-53 and 55-58 are pending and under examination. All rejections of record are withdrawn in view of Applicant's amendment and remarks. Claims 1, 9-15, 19, 41, 43-53 and 55-58 are allowed and have been renumbered as 1-25, respectively.

2. The following is an examiner's statement of reasons for allowance. The prior art cited neither teaches nor suggests a process for presenting a passenger peptide or polypeptide on the surface of a gram-negative host bacteria comprising: a) providing a host bacterium transformed with a vector encoding a polynucleotide operatively linked to a promoter wherein said polynucleotide comprises (i) a nucleotide sequence encoding a signal peptide, (ii) a nucleotide sequence encoding a passenger peptide or polypeptide, (iii) a nucleotide sequence encoding a protease recognition site, (iv) a nucleotide sequence encoding a transmembrane linker, and (v) a nucleotide sequence encoding a transporter domain of the AIDA protein *E. coli*, wherein the nucleotide sequence encoding the transporter domain is located downstream from the nucleotide sequence encoding the passenger peptide or polypeptide and (b) cultivating the host bacterium under conditions for inducing expression on the polynucleotide and presentation of the passenger peptide or polypeptide of (ii) on the surface of the host bacterium, wherein the passenger peptide or polypeptide of (ii) is heterologous in

relation to the transporter domain of (v) and the host bacterium is homologous to the transporter domain of (v)or recombinant vector obtained from the claimed method. The prior art cited also neither teaches or suggests a process for obtaining a library of bacteria expressing a variant population of surface-exposed passenger peptide or polypeptide, the process comprising: a) providing at least one vector comprising a chimeric gene obtained by cloning in frame, a nucleotide sequence encoding a signal peptide, a nucleotide sequence encoding passenger peptides or polypeptides and a nucleotide sequence encoding a transporter domain for an AIDA protein of *E. coli*, wherein the nucleotide sequence encoding the transporter domain is located downstream from the nucleotide sequence encoding the passenger peptide or polypeptide; b) mutagenizing the at least one vector to introduce variation into the nucleotide sequence encoding the passenger peptide or polypeptide; c) transfecting the at least one vector of step (b) into host bacteria capable of stably presenting the passenger peptide or polypeptide on the cell surface; d) expressing the chimeric gene in the host bacteria; e) culturing the host bacteria of step (d) to produce the passenger peptide or polypeptide stably exposed on the cell surface; f) selecting the host bacteria of step (e) with a surface-exposed passenger peptide or polypeptide, g) identifying and characterizing a binding partner for the surface-exposed passenger peptide or polypeptide of f), and wherein steps a) to g) are repeated several times in order to obtain the library of bacteria expressing the variant population of surface-exposed passenger peptides or polypeptides. The closest prior art is Georgiou et al (*U.S. Patent No. 5,348, 867 published September 20, 1994).* The prior art teaches a method that

results in a construct that is opposite in configuration to the construct obtained in the claimed method. The method of the prior art teaches a method for presenting peptides or polypeptides on the surface of gram-negative bacteria that results in C-terminal fusions and not N-terminal fusion as produced by the method of the prior art.

3. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (571) 272-8300.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov./>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vanessa L. Ford
Biotechnology Patent Examiner
May 1, 2006

NITA MINNIFIELD
PRIMARY EXAMINER
5-1-06

Examiner's Amendment

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Patrick T. Skacel on April 27, 2006.

The application has been amended as follows:

1. (Currently amended) A process for presenting a passenger peptide or polypeptide on the surface of Gram-negative host bacteria, comprising

a) providing a host bacterium transformed with a vector encoding a polynucleotide operatively linked to a promoter, wherein said polynucleotide comprises:

(i) a nucleotide sequence encoding a signal peptide,

(ii) a nucleotide sequence encoding a passenger peptide or polypeptide,

(iii) a nucleotide sequence encoding a protease recognition site,

(iv) a nucleotide sequence encoding a transmembrane linker, and

(v) a nucleotide sequence encoding a transporter domain of the Adhesin Involved in Diffuse Adherence (AIDA) protein of *E. coli*, wherein the nucleotide sequence encoding the transporter domain is located downstream from the nucleotide sequence encoding the passenger peptide or polypeptide; and

b) cultivating the host bacterium under conditions for inducing expression of the polynucleotide and presentation of the passenger peptide or polypeptide of (ii) on the surface of the host bacterium, wherein the passenger peptide or polypeptide of (ii) is heterologous in relation to the transporter domain of (v), and the host bacterium is homologous in relation to the transporter domain of (v).

2-8. Canceled.

9. (Previously presented) The process according to claim 1, wherein the passenger peptide has a length of 4-50 amino acids.

10. (Previously presented) The process according to claim 1, wherein the passenger polypeptide is of eukaryotic origin.

11. (Previously presented) The process according to claim 10, wherein the passenger polypeptide is an antibody or an antigen-binding domain of an antibody.

12. (Currently amended) The process according to claim 10, wherein the passenger polypeptide is the α chain of ~~an~~ a Major Histocompatibility Complex (MHC) class II molecule.

13. (Currently amended) The process according to claim 10, wherein the passenger polypeptide is the β chain of ~~an~~ a MHC class II molecule.

14. (Currently amended) The process according to claim 13, wherein the passenger polypeptide is the β chain of ~~an~~ a MHC class II molecule comprising an N terminus to which amino acids for binding are attached.

15. (Currently amended) The process according to claim ~~1~~ 41, wherein libraries of variant passenger peptides or polypeptides are expressed in host cells and presented on the host cell-surface, and wherein each host cell expresses one passenger variant.

16-18. (Canceled)

19. (Previously presented) The process according to claim 15, further comprising selecting single passenger peptides or polypeptides from one of said libraries.

20-40. (Canceled).

41. (Currently amended) A process for obtaining a library of bacteria expressing a variant population of surface-exposed passenger peptides or polypeptides, the process comprising:

a) providing at least one vector comprising a chimeric gene obtained by cloning in frame, a nucleotide sequence encoding a signal peptide, a nucleotide sequence encoding a passenger peptide or polypeptide, and a nucleotide sequence encoding a transporter domain for an AIDA protein of *E. coli*, wherein the nucleotide sequence encoding the transporter domain is located downstream from the nucleotide sequence encoding the passenger peptide or polypeptide;

b) mutagenizing the at least one vector to introduce variation into the nucleotide sequence encoding the passenger peptide or polypeptide;

c) transfecting the at least one vector of step (b) into host bacteria capable of stably presenting the passenger peptide or polypeptide on the cell surface;

d) expressing the chimeric gene in the host bacteria;

e) culturing the host bacteria of step (d) to produce the passenger peptide or polypeptide stably exposed on the cell surface;

f) selecting the host bacteria of step (e) with a surface-exposed passenger peptide or polypeptide,

g) identifying and characterizing a binding partner for the surface-exposed passenger peptide or polypeptide of f), and

wherein steps a) to g) are repeated several times <u>in order to obtain the library of bacteria expressing the variant population of surface-exposed passenger peptides or polypeptides</u>.

42. (Canceled).

43. (Previously presented) The process according to claim 41, wherein the passenger peptides or polypeptides have an affinity for a binding partner selected from the group consisting of a ligand, a receptor, an antigen, a toxin-binding protein, a protein with enzymatic activity, a nucleic acid-binding protein, an inhibitor, a protein having chelator properties, an antibody and an antigen-binding domain of an antibody.

44. (Previously presented) The process according to claim 41, wherein the bacteria expressing the surface-exposed passenger peptides or polypeptides have a binding affinity identified by binding to a labeled or unlabeled immobilized binding partner.

45. (Previously presented) The process according to claim 41, comprising introducing a modification into the binding partner of step g) wherein the modification is subsequently detected.

46. (Currently amended) The process according to claim 41, wherein the passenger peptide<u>s</u> or polypeptide<u>s</u> ~~is~~ <u>are</u> chemically or enzymatically modified on the bacterial surface.

47. (Previously presented) The process according to claim 46, wherein the modification is a non-covalent modification.

48. (Previously presented) The process according to claim 46, wherein the modification is a covalent modification.

49. (Currently amended) The process according to claim ~~48~~ 46, wherein the modification is a glycosylation.

50. (Currently amended) The process according to claim ~~48~~ 46, wherein the modification is a phosphorylation.

51. (Previously presented) The process according to claim 46, wherein the modification is a proteolysis.

52. (Previously presented) The process according to claim 51, wherein the passenger peptides or polypeptides are selectively released from the bacterial surface by endogenous or exogenous proteases.

53. (Previously presented) The process according to claim 52, wherein the passenger peptides or polypeptides are released by an endogenous protease of the host cell comprising OmpT protease, OmpK protease or protease X.

54. Canceled.

55. (Previously presented) A recombinant vector encoding a chimeric polynucleotide operatively linked to a promoter, the chimeric polynucleotide comprising:

a) a nucleotide sequence encoding a signal peptide,

b) a nucleotide sequence encoding a passenger peptide or polypeptide,

c) a nucleotide sequence encoding a protease recognition site,

d) a nucleotide sequence encoding a transmembrane linker, and

e) a nucleotide sequence encoding a transporter domain for an AIDA protein of *E. coli*, wherein the nucleotide sequence encoding the transporter domain is located downstream from the nucleotide sequence encoding the passenger peptide or polypeptide;

wherein the nucleotide sequence encoding the passenger peptide or polypeptide of b) is heterologous in relation to the nucleotide sequence encoding the transporter domain of e).

56. (Previously presented) A recombinant Gram-negative host bacterium, wherein the bacterium is transformed with a vector according to claim 55.

57. (Previously presented) A recombinant Gram-negative host bacterium transformed with a recombinant vector encoding a chimeric polynucleotide operatively linked to a promoter, the chimeric polynucleotide comprising:

a) a nucleotide sequence encoding a signal peptide,

b) a nucleotide sequence encoding a passenger peptide or polypeptide,

c) a nucleotide sequence encoding a protease recognition site,

d) a nucleotide sequence encoding a transmembrane linker, and

e) a nucleotide sequence encoding a transporter domain of the AIDA protein of *E. coli*, wherein the nucleotide sequence encoding the transporter domain is located downstream from the nucleotide sequence encoding the passenger peptide or polypeptide;

wherein the nucleotide sequence encoding the passenger peptide or polypeptide of b) is heterologous in relation to the nucleotide sequence encoding the transporter domain of e), and wherein the host bacterium is homologous in relation to the nucleotide sequence encoding the transporter domain of e).

58. (Previously presented) The host bacterium according to claim 57, wherein the bacterium is an *E. coli* cell.

59. Canceled.

CLEAN COPY OF CLAIMS

1. A process for presenting a passenger peptide or polypeptide on the surface of Gram-negative host bacteria, comprising

a) providing a host bacterium transformed with a vector encoding a polynucleotide operatively linked to a promoter, wherein said polynucleotide comprises:

(i) a nucleotide sequence encoding a signal peptide,

(ii) a nucleotide sequence encoding a passenger peptide or polypeptide,

(iii) a nucleotide sequence encoding a protease recognition site,

(iv) a nucleotide sequence encoding a transmembrane linker, and

(v) a nucleotide sequence encoding a transporter domain of the Adhesin Involved in Diffuse Adherence (AIDA) protein of *E. coli*, wherein the nucleotide sequence encoding the transporter domain is located downstream from the nucleotide sequence encoding the passenger peptide or polypeptide; and

b) cultivating the host bacterium under conditions for inducing expression of the polynucleotide and presentation of the passenger peptide or polypeptide of (ii) on the surface of the host bacterium, wherein the passenger peptide or polypeptide of (ii) is heterologous in relation to the transporter domain of (v), and the host bacterium is homologous in relation to the transporter domain of (v).

9. The process according to claim 1, wherein the passenger peptide has a length of 4-50 amino acids.

10. The process according to claim 1, wherein the passenger polypeptide is of eukaryotic origin.

11. The process according to claim 10, wherein the passenger polypeptide is an antibody or an antigen-binding domain of an antibody.

12. The process according to claim 10, wherein the passenger polypeptide is the α chain of a Major Histocompatibility Complex (MHC) class II molecule.

13. The process according to claim 10, wherein the passenger polypeptide is the β chain of a MHC class II molecule.

14. The process according to claim 13, wherein the passenger polypeptide is the β chain of a MHC class II molecule comprising an N terminus to which amino acids for binding are attached.

15. The process according to claim 41, wherein libraries of variant passenger peptides or polypeptides are expressed in host cells and presented on the host cell-surface, and wherein each host cell expresses one passenger variant.

19. The process according to claim 15, further comprising selecting single passenger peptides or polypeptides from one of said libraries.

41. A process for obtaining a library of bacteria expressing a variant population of surface-exposed passenger peptides or polypeptides, the process comprising:

a) providing at least one vector comprising a chimeric gene obtained by cloning in frame, a nucleotide sequence encoding a signal peptide, a nucleotide sequence encoding a passenger peptide or polypeptide, and a nucleotide sequence encoding a transporter domain for an AIDA protein of *E. coli*, wherein the nucleotide sequence encoding the transporter domain is located downstream from the nucleotide sequence encoding the passenger peptide or polypeptide;

b) mutagenizing the at least one vector to introduce variation into the nucleotide sequence encoding the passenger peptide or polypeptide;

c) transfecting the at least one vector of step (b) into host bacteria capable of stably presenting the passenger peptide or polypeptide on the cell surface;

d) expressing the chimeric gene in the host bacteria;

e) culturing the host bacteria of step (d) to produce the passenger peptide or polypeptide stably exposed on the cell surface;

f) selecting the host bacteria of step (e) with a surface-exposed passenger peptide or polypeptide,

g) identifying and characterizing a binding partner for the surface-exposed passenger peptide or polypeptide of f), and

wherein steps a) to g) are repeated several times in order to obtain the library of bacteria expressing the variant population of surface-exposed passenger peptides or polypeptides.

43. The process according to claim 41, wherein the passenger peptides or polypeptides have an affinity for a binding partner selected from the group consisting of a ligand, a receptor, an antigen, a toxin-binding protein, a protein with enzymatic activity, a nucleic acid-binding protein, an inhibitor, a protein having chelator properties, an antibody and an antigen-binding domain of an antibody.

44. The process according to claim 41, wherein the bacteria expressing the surface-exposed passenger peptides or polypeptides have a binding affinity identified by binding to a labeled or unlabeled immobilized binding partner.

45. The process according to claim 41, comprising introducing a modification into the binding partner of step g) wherein the modification is subsequently detected.

46. The process according to claim 41, wherein the passenger peptides or polypeptides are chemically or enzymatically modified on the bacterial surface.

47. The process according to claim 46, wherein the modification is a non-covalent modification.

48. The process according to claim 46, wherein the modification is a covalent modification.

49. The process according to claim 46, wherein the modification is a glycosylation.

50. The process according to claim 46, wherein the modification is a phosphorylation.

51. The process according to claim 46, wherein the modification is a proteolysis.

52. The process according to claim 51, wherein the passenger peptides or polypeptides are selectively released from the bacterial surface by endogenous or exogenous proteases.

53. The process according to claim 52, wherein the passenger peptides or polypeptides are released by an endogenous protease of the host cell comprising OmpT protease, OmpK protease or protease X.

55. A recombinant vector encoding a chimeric polynucleotide operatively linked to a promoter, the chimeric polynucleotide comprising:

a) a nucleotide sequence encoding a signal peptide,

b) a nucleotide sequence encoding a passenger peptide or polypeptide,

c) a nucleotide sequence encoding a protease recognition site,

d) a nucleotide sequence encoding a transmembrane linker, and

e) a nucleotide sequence encoding a transporter domain for an AIDA protein of *E. coli*, wherein the nucleotide sequence encoding the transporter domain is located downstream from the nucleotide sequence encoding the passenger peptide or polypeptide;

wherein the nucleotide sequence encoding the passenger peptide or polypeptide of b) is heterologous in relation to the nucleotide sequence encoding the transporter domain of e).

56. A recombinant Gram-negative host bacterium, wherein the bacterium is transformed with a vector according to claim 55.

57. A recombinant Gram-negative host bacterium transformed with a recombinant vector encoding a chimeric polynucleotide operatively linked to a promoter, the chimeric polynucleotide comprising:

a) a nucleotide sequence encoding a signal peptide,

b) a nucleotide sequence encoding a passenger peptide or polypeptide,

c) a nucleotide sequence encoding a protease recognition site,

d) a nucleotide sequence encoding a transmembrane linker, and

e) a nucleotide sequence encoding a transporter domain of the AIDA protein of *E. coli*, wherein the nucleotide sequence encoding the transporter domain is located downstream from the nucleotide sequence encoding the passenger peptide or polypeptide;

wherein the nucleotide sequence encoding the passenger peptide or polypeptide of b) is heterologous in relation to the nucleotide sequence encoding the transporter domain of e), and wherein the host bacterium is homologous in relation to the nucleotide sequence encoding the transporter domain of e).

58. The host bacterium according to claim 57, wherein the bacterium is an *E. coli* cell.